DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N-1502] 9233 '00 DEC 20 P4:03

Agency Information Collection Activities; Submission for OMB Review; Comment Request; Adverse Experience Reporting for Licensed Biological Products, and General Records

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that the proposed collection of information listed below has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments on the collection of information by [*insert date 30 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: JonnaLynn P. Capezzuto, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4659.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

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Adverse Experience Reporting for Licensed Biological Products; and General Records--21 CFR 600.12 and Part 600 Subpart D (OMB Control Number 0910-0308)--Extension

Under the Public Health Service Act (42 U.S.C. 262), FDA is required to ensure the marketing of only those biological products which are safe and effective. FDA must therefore be informed of all adverse experiences occasioned by the use of licensed biological products. FDA issued the adverse experience reporting (AER) requirements to enable FDA to take actions necessary for the protection of the public health in response to reports of adverse experiences related to licensed biological products. The primary purpose of FDA's AER system is to flag potentially serious safety problems with licensed biological products, focusing especially on newly licensed products. Although premarket testing discloses a general safety profile of a new drug's comparatively common adverse effects, the larger and more diverse patient populations exposed to the licensed biological product provides the opportunity to collect information on rare, latent, and long-term effects. Reports are obtained from a variety of sources, including patients, physicians, foreign regulatory agencies, and clinical investigators. Information derived from the AER system contributes directly to increased public health protection because such information enables FDA to recommend important changes to the product's labeling (such as adding a new warning), to initiate removal of a biological product from the market when necessary, and to ensure the manufacturer has taken adequate corrective action if necessary.

Section 600.80(c)(1) (21 CFR 600.80(c)(1)) requires the licensed manufacturer to report each adverse experience that is both serious and unexpected, regardless of source, as soon as possible but in any case within 15 working days of initial receipt of the information. Section 600.80(e) requires licensed manufacturers to submit a 15-day alert report obtained from a postmarketing clinical study only if there is a reasonable possibility that the product caused the adverse experience. Section 600.80(c)(2) requires the licensed manufacturer to report each adverse experience not reported under paragraph (c)(1) at quarterly intervals, for 3 years from the date of issuance of the product license, and then at annual intervals. The majority of the periodic reports will be

submitted annually since a large percentage of the current licensed biological products have been licensed longer than 3 years. Section 600.80(i) requires the licensed manufacturer to maintain for a period of 10 years records of all adverse experiences known to the licensed manufacturer, including raw data and any correspondence relating to the adverse experiences. Section 600.81 (21 CFR 600.81) requires the licensed manufacturer to submit information about the quantity of the product distributed under the product license, including the quantity distributed to distributors at an interval of every 6 months. The semiannual distribution report informs FDA of the quantity, the lot number, and the dosage of different products. Section 600.90 (21 CFR 600.90) requires a licensed manufacturer to submit a waiver request with supporting documentation when asking for waiving the requirement that applies to them under §§ 600.80 and 600.81.

Manufacturers of biological products for human use must keep records of each step in the manufacture and distribution of products including recalls of the product. The recordkeeping requirements serve preventative and remedial purposes. These requirements establish accountability and traceability in the manufacture and distribution of products, and enable FDA to perform meaningful inspections.

Section 600.12 (21 CFR 600.12) requires that all records of each step in the manufacture and distribution of a product be made and retained for no less than 5 years after the records of manufacture have been completed or 6 months after the latest expiration date for the individual product, whichever represents a later date. In addition, records of sterilization of equipment and supplies, animal necropsy records, and records in cases of divided manufacturing of a product are required to be maintained. Section 600.12(b)(2) requires complete records to be maintained pertaining to the recall from distribution of any product.

Respondents to this information collection are manufacturers of biological products. In fiscal year (FY) 99 there were approximately 79 licensed manufacturers. This number excludes those manufacturers who produce blood and blood components and in vitro diagnostic licensed products because they are specifically exempt from the regulations. However, not all manufacturers may

have any submissions in a given year and some may have multiple submissions. FDA received four waiver requests under § 600.90, of which one was approved for exemption of the AER requirements. In FY 99, there were an estimated 3,662 15-day alert reports, 13,238 periodic reports, and 502 distribution reports submitted to FDA. The number of 15-day alert reports for postmarketing studies as stated in § 600.80(e) was minimal and is included in the total number of 15-day alert reports. The hours per response are based on FDA experience. The burden hours required to complete the MedWatch Form for § 600.80(c)(1), (e), and (f) are reported under OMB Control No. 0910-0291.

In the Federal Register of September 25, 2000 (65 FR 57612), the agency requested comments on the proposed collection of information. No significant comments were received.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
600.80(c)(1) and (e)	78	46.95	3,662	1	3,662
600.80(c)(2)	78	169.72	13,238	1	13,238
600.81	78	6.4	502	1	502
600.90	4	1	4	1	4
Total					17,407

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

There are approximately 343 licensed manufacturers of biological products. However, the number of recordkeepers listed for § 600.12(a) through (e) excluding paragraph (b)(2) is estimated to be 111. This number excludes manufacturers of blood and blood components because their burden hours for recordkeeping have been reported under § 606.160 in OMB Control No. 0910-0116. The recordkeeping burden is based on the number of lots released (6,446), the number of recalls made (1,176), and the total number of AER reports received (16,900) for FY 99. The hours per record are based on FDA experience.

FDA estimates the burden of this recordkeeping as follows:

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Record-keeper	Total Hours
600.12	111	58.1	6,446	32	206,272
600.12(b)(2)	343	3.4	1,176	24	28,224
600.80(i)	79	213.92	16,900	1	16,900
Total					251,396

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

Dated: December 18, 2000

Margaret M. Dotzel,
Associate Commissioner for Policy.

[FR Doc. 00–????? Filed ??–??–00; 8:45 am]

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